Injury 53 (2022) 49–53

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Massive transfusion protocols in the Netherlands. Consensus or confusion?

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ARTICLE INFO

Article history:
Accepted 29 October 2021

Keywords:
Massive transfusion
Trauma
Resuscitation
Massive transfusion protocol
Haemorrhage
Shock
Bleeding
Damage control resuscitation
Platelets

ABSTRACT

Introduction: Transfusion strategy for trauma patients with massive haemorrhage is often incorporated in massive transfusion protocols (MTP). Albeit correct MTP use results in better patient outcome, research regarding the state of MTP knowledge is scarce. The objective of this study is therefore to assess knowledge of local MTP and massive transfusion strategy in the level 1 trauma centres in the Netherlands. Our hypothesis is that actual MTP knowledge is low and transfusion strategy differs.

Materials and methods: Surveys were sent out in January 2020 to all trauma and vascular surgeons, anaesthesiologists, emergency department physicians of the largest level 1 trauma centre (locally, $n = 113$) and to one trauma surgeon, emergency physician and anaesthesiologist in each of the nine other governmentally assigned level 1 trauma centres in the Netherlands (nationally, $n = 27$). The respondents were subdivided into a frequent user group (MTP usage $\geq$ 4 times in 2019) and a non-frequent user group (MTP usage $<$ 4 in 2019). Data are expressed as numbers and percentages.

Results: Response rate was ($n = 48$; 42%) for the local survey and ($n = 14$; 52%) for the national survey. Locally, ($n = 23$; 48%) and ($n = 25$; 52%) respondents were defined frequent and non-frequent users respectively and national respondents all as frequent users. In total, ($n = 13$; 27%) of local respondents were aware of the current local composition of the MTP. Respondents indicated to transfuse erythrocytes first, followed by plasma and platelets (local non-frequent users $n = 23$; 92%, local frequent users $n = 21$; 91% and national frequent users $n = 13$; 93%). The indication for platelet transfusion was units erythrocytes transfused (local non-frequent users $n = 10$; 40% frequent users locally $n = 11$; 48% and nationally $n = 5$; 36%) and clinical view (local non-frequent users $n = 9$; 36%, frequent users locally $n = 8$; 35% and $n<5$ nationally. Whereas few respondents claimed ($n = 5$; 21% non-frequent users locally and $n <5$ nationally) to transfuse platelets based on platelet counts. Viscoelastic haemostatic assays were performed during MTP, but only by frequent users.

Conclusion: The majority of physicians dealing with massive transfusion in trauma patients were not aware of the exact composition of the MTP and consensus regarding transfusion strategy and indication for platelet transfusion was low.

Introduction

Death by traumatic injury is in approximately 20–40% of the cases caused by haemorrhage which is often preventable by adequate bleeding control and damage control resuscitation (DCR). [1,2] Despite improved pre-hospital care, innovated early haemorrhage control and increased knowledge regarding trauma induced coagulopathy (TIC), mortality only slightly decreased in the

Abbreviations: DCR, Damage control resuscitation; MTP, Massive transfusion protocol; TIC, Trauma induced coagulopathy.

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https://doi.org/10.1016/j.injury.2021.10.034

past decade. [3] The introduction of massive transfusion protocols (MTP) years ago to streamline transfusion during DCR proved to be an important step in situations with uncontrolled haemorrhage. Partly by military experiences from recent conflicts that have led to new insights on DCR, thereby shifting from liberal transfusion of red blood cells (RBC) and crystalloids to a more balanced resuscitation with RBCs, plasma and platelets in a ratio mimicking whole blood. [4] Despite having MTPs available in most hospitals, content is still variable, even after a 10-year period as these MTPs are dynamic and new knowledge has led to new insights. [5–7] Additionally, the possible role of adjuncts such as fibrinogen concentrate or cryoprecipitate has been increasingly recognized in recent years. [8,9] Despite availability of a national guideline in the Netherlands, MTP content in all level 1 trauma centres is varying and whether transfusion practice is concordant with local MTP or is driven by expert opinion or other guidelines is currently not known. [10] Albeit the evidence that early and correct MTP use results in improved coagulation, survival benefit and cost reduction, it is expected that actual knowledge regarding the correct MTP strategy is low. [5,11-14] The aim is to determine MTP knowledge and massive transfusion strategy for trauma patients. We hypothesise that MTP knowledge is low and strategies vary.

Materials and methods

This study was exempt from review by the medical ethical committee Rotterdam. An anonymously online survey was sent to all physicians prone for dealing with the MTP in Erasmus Medical Centre, Rotterdam (EMC) (from here: local survey). An second, identifiable survey was send to three invited professionals in each of the nine other governmentally assigned level 1 trauma centres in the Netherlands (from here: national survey). Only respondents with high probability of dealing with MTP activation for trauma patients were invited. Obstetricians, intensivists, haematologists and general surgeons, were therefore excluded from participation. Local respondents were subdivided into an MTP frequent group (actual MTP use $\geq$ 4 times in 2019) and an MTP non-frequent group ($<$ 4 actual MTP use in 2019). The survey was designed using the online tool LimeSurvey (LimeSurvey Project Hamburg, Germany), approved for use by the EMC. After one, two and three weeks, reminders were sent to non-responders. The survey included questions regarding baseline characteristics of the participants, the composition of the local MTP, use of viscoelastic haemostatic assays during transfusion and the transfusion strategy for platelets. (Appendix S1). Both surveys were sent in January 2020.

Local survey: within all departments of one level 1 trauma centre

With approximately 400–500 admitted severely injured trauma patients (with injury severity score of $\geq$ 16) and 160 MTP activations, annually this level 1 trauma centre has the highest polytrauma patient load in the Netherlands. [10] A total of 113 surveys were sent to potential local respondents situated in the departments of surgery (n = 33), anaesthesiology (n = 50) and the emergency department (ED) (n = 30).

National survey: expert opinion in other level 1 trauma centres

To obtain an impression of MTP use on a national level, an identical survey was sent to one trauma surgeon, anaesthesiologist and emergency department physician in the other governmentally assigned level 1 trauma centres in the Netherlands (Groningen, Zwolle, Enschede, Amsterdam (2x), Leiden, Nijmegen, Tilburg, Maastricht) (n = 27)

Statistics

All data were exported and analysed using SPSS version 27. Data were expressed as numbers and percentages. To avoid identification back to the individual, only percentages and numbers of groups with $\geq$ 5 respondents were reported. Groups with $<$ 5 respondents were only reported as such.

Results

Respondents

Only fully completed surveys were included in the analysis which resulted in a total of (n = 48; 42%) responses for the local survey and (n = 14; 52%) for the national survey. Responses for the local survey were received from the department of anaesthesiology (n = 17/50; 34%), emergency medicine (n = 7/30; 23%) and surgery (n = 16/33; 48%). Six respondents (13%) were working part-time at the helicopter emergency medicine service (HEMS) and/or Ministry of Defence (MoD). For the national survey, respondents were trauma or vascular surgeons (n = 5/14; 36%), anaesthesiologists (n<5) or ED physicians (n = 5/14; 36%). Of these respondents, (n = 7/14; 50%) were working at the HEMS or MoD. (Table 1)

Massive transfusion practice

Local respondents were defined as non-frequent users (n = 25; 52%) and frequent users (n = 23; 48%). National respondents were all defined frequent users (n = 14). In the context of MTP activation, local and national frequent users activate MTP more often in comparison to local non-frequent users. Locally, (n = 7; 28% of the non-frequent users and n = 6; 26% of frequent users) indicated to be aware of the correct local composition of the current MTP packages (2:2 followed by 2:2:1 or 4:4:1). Local respondents referred to the 3:3:1 package used until February 2019 (non-frequent users n = 9; 36%, local frequent users n = 10; 43%) (Fig. 1a).

Respondents indicated to transfuse RBCs first (local non-frequent users n = 23; 92%, local frequent users n = 21; 91%, and national frequent users n = 13; 93%), followed by plasma or platelets first (in all groups n < 5) (Fig. 1b). National frequent users (n = 6; 43%) indicated that MTP packages were on location within 5–10 min followed by respondents that indicated arrival in less than 5 min, 10–15 min, or even after 20 min (in all groups n <5). The other results regarding type and screening prior to actual MTP transfusion, use of viscoelastic haemostatic assays and cell saver use are summarized in Fig. 1c and 1d and appendix S2.

Platelet transfusion during massive transfusion

An overview of the results regarding platelet transfusion during MTP use are shown in Fig. 2 and appendix S3. For the question regarding the timing of platelet transfusion, most respondents indicated to transfuse platelets within 16–30 min after MTP activation (local non-frequent users n = 8; 32%, local frequent users n = 10; 43% and national frequent users n = 7; 50%) (Fig. 2A). The indication for platelet transfusion was based on total units of RBCs (local non-frequent users n = 10; 40%, local frequent users n = 11; 48% and national frequent users n = 5; 36%) and by clinical view (local non-frequent users n = 9; 36%, local frequent users n = 8; 35% and national frequent users n<5). Local non-frequent and national respondents claimed to use platelet count as indication for platelet transfusion (n = 5; 20% and n<5). Although many respondents claimed to use viscoelastic testing during MTP, local non-frequent users did not use viscoelastic haemostatic assays to guide

Table 1
Characteristics of survey participants.

	Local		National
	Non-frequent users $n = 25$	Frequent users $n = 23$	Frequent users $n = 14$
Surgeons	< 5	5 (22)	5 (36)
Anaesthesiologists	10 (40)	7 (30)	< 5
ED physician	< 5	6 (26)	5 (36)
Residents	11 (44)	5 (22)	n/a
Ministry of Defence / HEMS	< 5	< 5	7 (50)

Data are presented as number (n) and percentage (%).
ED, emergency department; HEMS, helicopter emergency medical services; n/a, not applicable.
Frequent users were defined as actual MTP use of ≥ 4 times in 2019.

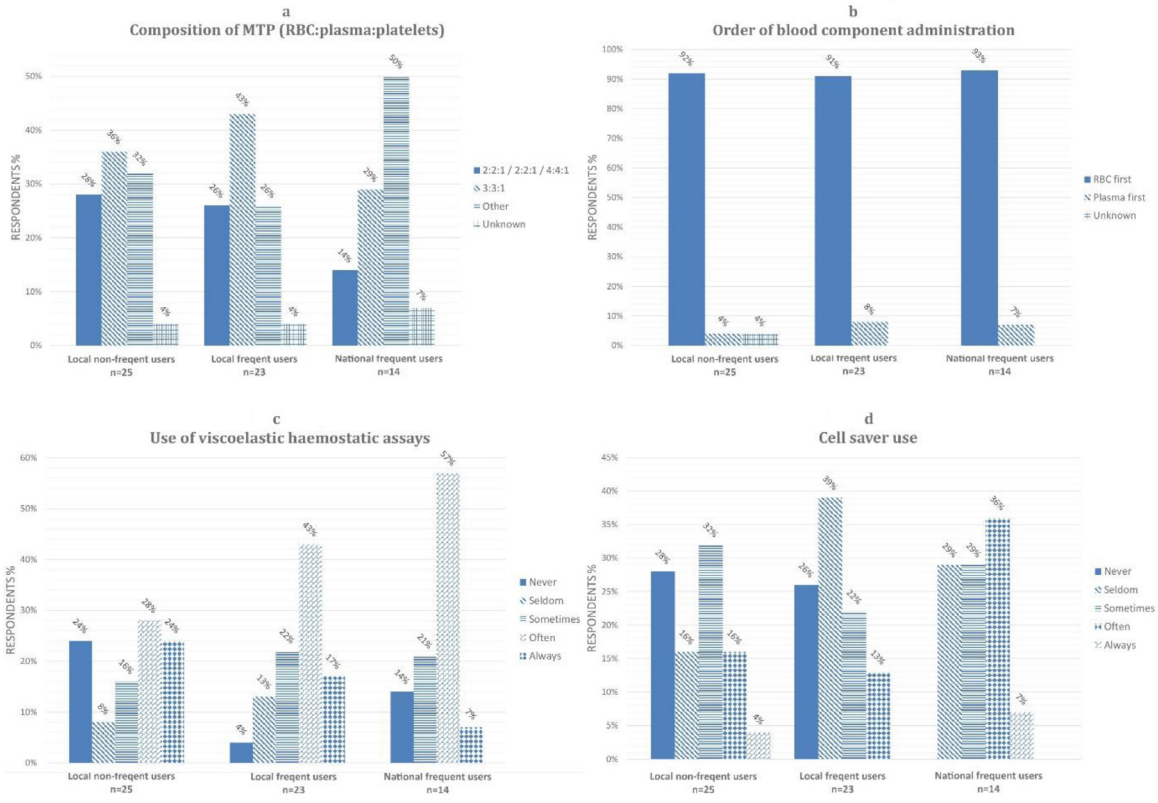

Fig. 1. Massive transfusion protocol content and transfusion strategy.

platelet transfusion and $n<5$ of respectively local and national frequent users did (Fig. 2B).

Discussion

A low percentage of respondents was aware of the exact MTP composition and massive transfusion strategy. Since correct use of the MTP can result in a survival benefit, a reduction in blood components use and accompanied cost savings, these results are important. [5,11,15]

Since MTPs in all level 1 trauma centres differ, it was expected to find inter-hospital variation. However, also in the local survey, variation was found. There are several explanations for both the demonstrated local variation in claimed transfusion strategy. First, it is imaginable that local respondents were only aware of the outdated MTP (revised in February 2019 and added in appendix S4). Secondly, the complexity of the local MTP may have contributed to the variance and finally frequent users may mainly transfuse based on experience and not 'protocol' based. The reason for this observed variation could however not be answered by the results of this survey.

Furthermore the indication for platelet transfusion varied, the majority of respondents claimed to transfuse platelets mainly based total units' RBCs or clinical view. The former is compliant with (inter)national guidelines in which is advised to transfuse platelets in balanced ratios during the 'blind' uncontrolled phase of transfusion and not based on platelet counts. [4,9,16-18] In addition to the blind phase of resuscitation, viscoelastic haemostatic assays and administration of additional medication such as fibrinogen concentrate, tranexamic acid and prothrombin complex concentrate are currently embedded in most MTPs to timely prevent, recognize and treat TIC. [19] It appears that viscoelastic haemostatic assays are used during MTP although rarely as indication for platelet transfusion. This may suggest that more training is required to use these type of assays during MTP. However, this may be complicated as assay protocols differ between institutes and the added value of viscoelastic haemostatic assays in comparison with traditional laboratory tests during massive transfusion in trauma patients still remains to be shown. [19]

The lack of uniformity in MTP we showed in our study is in line with the study of Treml et al. which also showed differences in MTPs between centres. [20] An explanation for the differences

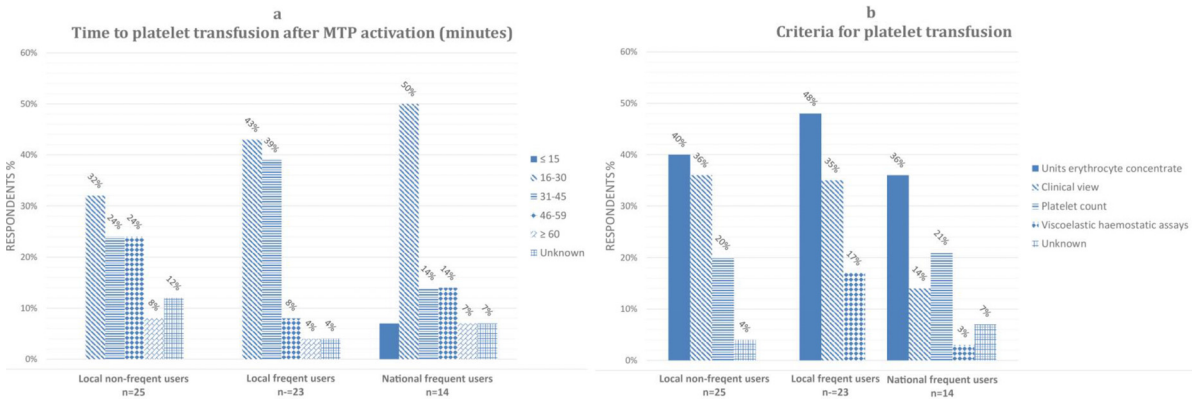

Fig. 2. Platelet transfusion.

in transfusion practice between centres may also be explained by differences in local blood bank logistics. It is known that not all participating hospitals have thawed plasma (shelf life 2–5 days at 4 °C) readily available for transfusion because in these hospitals continuous availability of thawed AB plasma would result in unnecessary spillage of precious products due to expiration. As a result, it is often not possible transfuse all blood products early in a balanced way and the patient receives relatively more erythrocyte concentrate than plasma or platelets during early treatment. Experiences and knowledge from the military with readily available longer shelf-life plasma such as spray or freeze-dried plasma (shelf life 1–2 years) and thawed −80 °C plasma (shelf life 14 days) may offer solutions to be able to transfuse early in a more balanced way. [21,22]

With these results we aim to create awareness amongst clinicians that MTP content and strategy varies on both a local and national level. We hope these results will encourage clinicians to analyse their own hospital-specific MTP and convey the importance to all potential users, both frequent and non-frequent users. Whether MTP strategy effects patient outcome was beyond the scope of this study but is currently investigated by this study group in a national multicentre study. Preferably there is consensus on both local and national level with periodic revision of the MTP according to (inter)national guidelines. Since knowledge comes with frequent use or training, clinicians from departments prone for dealing with MTPs (surgery, anaesthesiology and emergency) should be additionally trained in local MTP strategy and logistics. Currently, MTP education is not yet or hardly implemented. Ideally, an MTP is both online as hard copy (in the trauma bay) available and repeated training is provided.

Strength and limitations

There are limitations to this study. First, since these results are an estimation and only opinion based, it is imaginable that actual practice will be different. Whether actual transfusion is expert or protocol (local, national or international) based and/or subjected to variability in knowledge and practice and whether this has led to differences in patient outcome, could not be identified with this study. Secondly, in this study a physician using the MTP four times annually was defined to be a frequent user and the question arises whether this threshold should be higher. Finally, the response rate is fairly low (42% for the local survey and 52% for the national survey). On the other hand, a strength of this study is that on the local level all professionals that are involved in trauma care prone for dealing with massive transfusion / MTP were included. Furthermore, a great strength is its national rollout to frequent users in all level 1 trauma centres, expected to provide an adequate overview about MTP strategy in trauma care in the Netherlands. Besides research to the current use and effect of MTP, future research should focus on implementation of education and training and determining the added value of education and training to increase MTP adherence during vital stages of resuscitation and the effect(s) on patient outcome.

Conclusion

Knowledge of MTPs and transfusion strategy is low in both frequent and non-frequent MTP users. Additionally, viscoelastic haemostatic assays are used more often by frequent users, RBCs are mainly transfused first and platelet transfusion is based on total number of RBCs or on clinical view. We hope these results encourage clinicians to analyse their own MTP content and strategy.

Declaration of Competing Interest

None

Source of funding

Dutch Department of Defence and the Dutch Army Health Insurance Foundation (SZVK).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.injury.2021.10.034.

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